

MASSIVE BLOOD TRANSFUSION

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Priorities in massive transfusion

- 1 Replace and maintain blood volume
- 2 Maintain haemostasis:
Platelet count ($>50 \times 10^9/l$)
Coagulation factors
- 3 Optimise oxygen carrying capacity:
Maintain packed cell volume >20
- 4 Correct or avoid metabolic disturbances:
Hypocalcaemia
Hyperkalaemia
Acid-base disturbance
Hypothermia
- 5 Maintain plasma colloid osmotic pressure

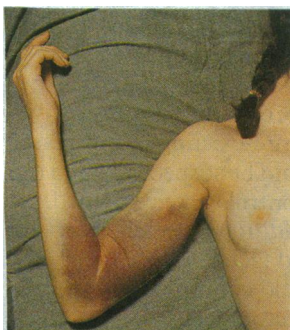
"Massive transfusion" is arbitrarily defined as the replacement of the patient's total blood volume by stored homologous bank blood in less than 24 hours. It is a medical emergency, usually occurring in the accident department, the operating theatre, or the obstetric department, when a patient presents with overwhelming haemorrhage and acute hypovolaemic shock. Rapid loss of large quantities of blood impairs tissue perfusion and requires urgent correction. Management comprises prompt resuscitation to maintain circulating blood volume, the oxygen carrying capacity of blood, haemostasis, colloid osmotic pressure, and plasma biochemical balance.

The morbidity and mortality from massive transfusion are high, not because of the transfusion itself but because of the underlying reason for the haemorrhage and any pre-existing diseases. Patients who have massive haemorrhages do not form a uniform group and cannot be expected to behave in similar ways. Prolonged shock, hypotension, extensive tissue damage, and obstetric complications can all predispose to disseminated intravascular coagulation, which must be recognised and treated. Pre-existing liver or renal disease can exacerbate the complications of massive transfusion, as there may already be abnormalities of haemostasis or plasma protein concentrations, and some of the elements of the transfused blood may not be metabolised in the normal way.

Management

Minimum laboratory investigations in patients with acute hypovolaemic shock

- Blood transfusion (10 ml clotted blood):
For ABO and Rh D group
- Haematology (2 ml in EDTA):
Haemoglobin concentration or packed cell volume
Platelet count
- Coagulation (5 ml in citrate):
Thrombin time
Prothrombin time
- Biochemistry:
Baseline urea and electrolyte concentrations



Patient with large ecchymosis resulting from disseminated intravascular coagulation.

• Blood volume

The most important factor in the management of hypovolaemic shock is to restore the circulating blood volume as rapidly as possible. Profound or prolonged hypotension will exacerbate damage to tissues or organs and predispose to disseminated intravascular coagulation. Mortality after massive transfusion increases with the duration and severity of the shock.

Blood volume may initially be restored with crystalloid and synthetic colloid solutions. As soon as blood loss and fluid replacement reach 40% of blood volume, replacement of red cells is required. Although red cells or red cells suspended in additive solutions can initially be used, it is preferable to use whole blood after the first four units of a massive transfusion (eight or more units) because the plasma will provide both the coagulation factors and the protein needed to maintain haemostasis and colloid osmotic pressure, respectively.

As soon as the need for massive transfusion is recognised, blood samples should be taken for certain minimal laboratory tests, the results of which will be available within 15 minutes.

• Blood transfusion

The blood transfusion laboratory should be informed of the expected need for massive transfusion and the urgency for transfusion. If time permits the ABO and Rh D group of the recipient should be determined and an antibody screen and compatibility test carried out. If blood is required more urgently then a specific request for uncrossmatched blood should be made by the clinician. In obstetric and surgical cases the blood group will

**UNCROSSMATCHED BLOOD
ABO + Rh(D) HOMOLOGOUS**

SURNAME

FIRST NAMES

HOSP. REG. No.

D.O.B.

WARD

PATIENTS GROUP

DATE REQUIRED

Examples of warning labels attached to uncrossmatched blood.

UNCROSSMATCHED BLOOD

SURNAME

FIRST NAMES

HOSP. REG. No.

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Characteristics of microvascular bleeding

- Bleeding from mucous membranes
- Bleeding from catheter and venepuncture sites
- Oozing from raw surfaces
- Generalised petechiae
- Increasing size of ecchymoses.

usually be known and an antibody screen will have already been carried out; ABO and Rh D compatible blood can then be issued even if a rapid compatibility test cannot be done. In cases of trauma in which the blood group of the patient is not known it may (rarely) be necessary to start the transfusion with group O blood while the ABO group is ascertained. A switch to ABO specific blood should then be made as soon as possible to (a) avoid inappropriate use of group O blood and (b) to reduce the amount of group O plasma transfused to a non-O recipient.

The combination of shock, sepsis, tissue injury, and massive transfusion often culminates in the adult respiratory distress syndrome, and transfused microemboli from white cell and platelet aggregates may contribute to its development. Unfortunately micropore filters (between 20 and 40 μm) are no more effective than standard blood filters (pores 170 μm), as they impede the flow of blood and become occluded and useless after the first unit of blood has been filtered.

The use of uncrossmatched "fresh" blood from "walk in" donors is a dangerous practice because the units will not have been screened for transmissible viral agents and because component treatment (outlined below) will control specific haemostatic defects more efficiently.

• *Haemostasis and component treatment*

Stored blood undergoes progressive losses, mainly of factors V and VIII; factor VIII decreases to roughly 50% after the first day, 30% after five days, and 6% after 21 days. Factor V activity falls to 50% after 14 days. There is no appreciable loss of the other coagulation factors until blood has been stored for 21 days. Platelet function, however, is quickly lost, and after storage for 48 hours there are practically no functioning platelets left. If plasma reduced cells or red cells suspended in an optimal additive solution are transfused, coagulation factors will be reduced. Infusion of crystalloid solutions, human albumin preparations, or one of the artificial colloid substitutes will cause further dilution of coagulation factors and platelets and may occasionally cause additional interference with haemostatic mechanisms. The various red cell preparations may also precipitate disseminated intravascular coagulation by a combination of partial activation of clotting factors and the breakdown of platelets, leucocytes, and red cells (which release thromboplastin-like material during storage). There is also evidence that platelet function may be impaired in patients having massive transfusions.

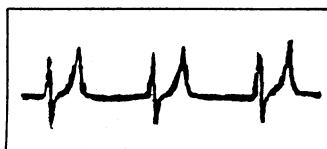
In the past, standardised regimens of platelet concentrates and fresh frozen plasma have often been given after the equivalent of one blood volume (about 8-10 units of blood in an adult) has been transfused. To prevent indiscriminate use of components, however, patients having massive transfusions should have routine tests of haemostasis monitored early to define their precise abnormalities. These patients are most likely to develop microvascular bleeding with oozing from the mucosa, raw wounds, and puncture sites as a result of thrombocytopenia (platelet count $<50 \times 10^9/\text{l}$) when one and a half to twice their blood volume has been replaced. Thrombocytopenia may be aggravated by increased consumption of platelets. A standard adult dose of six to eight units of platelet concentrate should be infused to control this microvascular bleeding, roughly equivalent to one unit of concentrate/10 kg body weight. Each unit of platelet concentrate contains a minimum of 0.55×10^{11} platelets and 50 ml plasma. Using these rough guidelines the amount of platelet concentrate needed can usually be predicted as the volume replacement requirements increase.

Generally the haemostatic concentrations of the coagulation factors are well maintained and fresh frozen plasma is not needed prophylactically. Fresh frozen plasma should be restricted to controlling defined defects in the coagulation cascade with prolongation of the prothrombin time by five seconds or more, which is usually associated with pre-existing liver disease. Acute disseminated intravascular coagulation should be suspected when the thrombin time extends to more than double the control value. About 10 units of cryoprecipitate should then be given in addition to fresh frozen plasma to correct the deficiencies of fibrinogen and factor VIII.

The need for future haemostatic treatment should continue to be monitored by clinical response and repeated laboratory tests.



Empty cryoprecipitate packs.



Electrocardiograph changes of hyperkalaemia

- ☐ Peaked T waves
- ☐ Disappearance of P waves
- ☐ Broadened QRS complex
- ☐ Slurring of ST segment into T waves
- ☐ Sine wave leading to cardiac arrest

• Oxygen carrying capacity

Modern anticoagulant preservative solutions (for example, citrate phosphate dextrose adenine) for red cells ensure adequate concentrations of 2, 3-diphosphoglycerate and therefore of oxygen carrying capacity for up to 14 days after collection of the blood. Reduced oxygen carrying capacity is likely to be important only in patients with pre-existing cardiac disease or severe anaemia. It is sensible, however, to use blood that is less than 14 days old.

• Metabolic disturbances

Hypocalcaemia is theoretically a problem, but clinical consequences are rare and complications as a result of calcium given "prophylactically" are possibly more harmful than hypocalcaemia.

Hyperkalaemia is usually transient and unimportant. The combination of hypocalcaemia and hyperkalaemia, exacerbated by hypothermia caused by rapid transfusion of blood stored at 4°C, however, can cause cardiac irregularities and electrocardiographic monitoring is advisable.

Citrate toxicity is unlikely to be a problem. Unless there is liver dysfunction, citrate is metabolised rapidly; transfusion rates of one unit of blood every five minutes must be exceeded before the citrate metabolism is overwhelmed.

Although stored blood has a reduced pH, *acidosis* in recipients of massive transfusions is rare because metabolism of citrate produces an alkalosis. Routine use of alkalinising agents should therefore be avoided. Prolonged hypoperfusion and shock are more likely to cause acidosis; the need for alkalinising agents should be judged by the results of laboratory tests and not by the number of units of blood transfused.

• Plasma colloid osmotic pressure

Replacement of massive blood loss with large volumes of crystalloids, synthetic colloids, and red cell preparations devoid of plasma will lead to a fall in plasma colloid osmotic pressure. This may contribute to the development of the adult respiratory distress syndrome, and transfusion of albumin may be necessary if plasma albumin concentrations fall appreciably.

Conclusion

The examples of warning labels are reproduced by kind permission of Dr H Dodsworth.

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Traditional regimens for managing massive transfusion include routine use of supplements like fresh frozen plasma or platelets, or both, alkalinising agents, and calcium supplements, all in fixed quantities according to the amount of blood transfused. This is wasteful, possibly dangerous, and often unnecessary. The need for supplements should be judged by careful clinical assessment and frequent laboratory measurements, so that each patient receives the optimum treatment.

ANY QUESTIONS

Is it known whether habitual physical exercise into middle age in men has a protective effect against prostatic disorders, especially benign hypertrophy? Is there any evidence for a hormonally mediated effect?

Little has been written about the relation between prostatic disease and physical exercise. Epidemiological studies suggest an inverse relation between exercise and the incidence of carcinoma of the prostate.¹ A similar relation exists with other malignant tumours such as those of the breast and colon.² There are, however, no such data relating to benign prostatic disease.

One study measured the effect on male endocrinology of 48 hours of physical exercise. There was a significant rise in oestrogen concentrations followed by a smaller secondary fall in the concentrations of circulating androgens.³ Benign prostatic hyperplasia and carcinoma of the prostate are hormone dependent diseases. Neither condition occurs in men castrated before puberty, and both benign prostatic hyperplasia and carcinoma respond to withdrawal of androgens. The aetiology of benign prostatic hyperplasia seems to be related to the accumulation of dihydrotestosterone

within the prostate. The action of this hormone is enhanced by oestrogens, which increase the amount of androgen receptor within the gland. Thus rising concentrations of oestrogens in elderly men may allow the development of benign prostatic hyperplasia despite a fall in the production of testosterone over the age of 60.⁴

Regular exercise, especially for short periods, may create a suitable hormonal environment for the development of benign prostatic hyperplasia. Data supporting such a hypothesis, however, are lacking, and whether physical exercise is a factor influencing the development of benign prostatic hyperplasia must remain open to question.—J G GINGELL, consultant urologist, and D CHADWICK, research registrar, Bristol

1 Yu H, Harris RE, Wynder EL. Case control study of prostate cancer and socioeconomic factors. *Prostate* 1988;13:317-25.

2 Albanes D, Blair A, Taylor PR. Physical activity and the risk of cancer in the NHANES I population. *Am J Public Health* 1989;79:744-50.

3 Friedl KE, Plymate SR, Bernhard WN, Mohr LC. Elevation of plasma estradiol in healthy men during a mountaineering expedition. *Horm Metab Res* 1988;10:239-42.

4 Wilson JD. The pathogenesis of benign prostatic hyperplasia. *Am J Med* 1980;68:745-56.